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<b>(21) International Application Number:</b> PCT/US97/11932 <b>(22) International Filing Date:</b> 8 July 1997 (08.07.97)  <b>(30) Priority Data:</b> <table border="0" style="width: 100%;"><tr><td style="width: 30%;">08/688,448</td><td style="width: 40%;">30 July 1996 (30.07.96)</td><td style="width: 30%;">US</td></tr><tr><td>08/688,445</td><td>30 July 1996 (30.07.96)</td><td>US</td></tr><tr><td>08/815,779</td><td>12 March 1997 (12.03.97)</td><td>US</td></tr><tr><td>08/873,792</td><td>12 June 1997 (12.06.97)</td><td>US</td></tr></table> <b>(71) Applicant:</b> ENERGETICS, INC. [US/US]; Suite 2C, 1095 Park Avenue, New York, NY 10128 (US). <b>(72) Inventors:</b> JACKSON, Sherry, D.; Suite 2C, 1095 Park Avenue, New York, NY 10128 (US). BLUMBERG, Jeffrey, B.; 117 Nonantum Street, Newton, MA 02158 (US). <b>(74) Agents:</b> TSEVDOS, Estelle, J. et al.; Kenyon & Kenyon, One Broadway, New York, NY 10004 (US).		08/688,448	30 July 1996 (30.07.96)	US	08/688,445	30 July 1996 (30.07.96)	US	08/815,779	12 March 1997 (12.03.97)	US	08/873,792	12 June 1997 (12.06.97)	US	<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>
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<b>(54) Title:</b> DIETARY SUPPLEMENTS  <b>(57) Abstract</b> <p>The present invention relates to dietary supplements for supplementing the dietary needs of women and preventing or reducing life stage associated health risks during each of their principal adult life stages (pre-perimenopause, perimenopause and menopause, or post-menopause). It also relates to a method of supplementing the dietary needs of women whereby an effective amount of a life stage appropriate dietary supplement is administered to a woman at each of her life stages throughout her life. The present also relates to dietary supplements for supplementing the specific phytochemical dietary needs of perimenopausal and menopausal women which contain low doses of phytoestrogens, and a method for such dietary supplementation.</p>														

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### DIETARY SUPPLEMENTS

5        This application is a continuation-in-part  
application of application Serial Number 08/688,448 filed  
on July 30, 1996.

#### 10                    **FIELD OF THE INVENTION**

The present invention relates to dietary  
supplements. More particularly, it relates to dietary  
supplements formulated to supplement a woman's specific  
micronutrient and phytochemical needs during each of her  
15    adult life stages, thereby promoting her well being and  
preventing or reducing the health risks to which she is  
exposed.

#### **BACKGROUND OF THE INVENTION**

20        The nutritional and health needs of women differ in  
many respects from those of men. Moreover, they vary  
with each developmental or life stage. For women, in  
particular, each adult life stage poses wide ranging  
nutritional requirements that significantly affect the  
25    health risks to which they are exposed.

In general, women pass through three principal adult

developmental or life stages - the childbearing or pre-perimenopausal stage; the perimenopausal and menopausal stage; and the post-menopausal stage. Numerous health conditions and risks may develop during each of these  
5 life stages. They include coronary heart disease (CHD), some cancers, cervical dysplasia, menopause, osteoporosis, pre-menstrual syndrome (PMS), iron deficiency anemia, and fetal neural tube defects. The incidence of these conditions and risks varies with each  
10 life stage and has been shown to be influenced by diet and dietary supplements.

CHD is a major cause of death in women. It claims the lives of nearly 250,000 women per year, most of whom  
15 are post-menopausal. Although generally not manifest until the post-menopausal stage, CHD develops over decades. Well established risk factors for CHD include elevated plasma cholesterol levels and abnormal glucose metabolism. Also implicated in the development of CHD  
20 are elevated homocysteine levels and the effects of free radicals. Phytoestrogens, antioxidants, chromium and folic acid have been shown to mitigate these risk factors.

25 In general, the risk of cancer increases with age. Breast cancer, which afflicts one in every nine women, is chief among women's concerns. Both antioxidants and phytoestrogens appear to have a role in the prevention of some cancers, particularly breast cancer. Furthermore,  
30 folic acid has been shown to reduce the risk of cervical dysplasia, which is a precursor to cervical cancer.

Menopause can result in various unpleasant symptoms, including hot flashes, night sweats, mood swings,  
35 insomnia and fatigue. Phytoestrogens have been shown to

reduce these symptoms.

Osteoporosis is associated with the aging process and predominantly affects women. It is characterized by  
5 diminished bone density, which results in increased bone fractures and vertebral column collapse. Bone loss begins around age 35. This loss accelerates during the menopause, which generally occurs around age 45 to 55. Osteoporosis develops over decades and is related to peak  
10 bone mass, as well as to the degree of bone loss. Adequate calcium intake prevents osteoporosis. Moreover, certain vitamins and minerals enhance calcium absorption and utilization.

15 PMS is a common recurring multi-symptom condition experienced by many menstruating women. Symptoms include water retention, breast tenderness, headaches, mood swings, etc. Vitamin B<sub>6</sub> has been shown to reduce some of these symptoms.

20 Iron deficiency anemia is also prevalent in women, particularly in menstruating women, but can also be found among elderly women. Treatment of iron-deficiency anemia generally consists of iron supplementation. Iron,  
25 however, is not readily absorbed and can cause constipation, particularly in the elderly. The presence of vitamin C in adequate amounts increases the bioavailability of iron.

30 Fetal neural tube defects may occur during the first month of gestation, often before a woman is aware of her pregnancy. Folic acid prevents fetal neural tube defects and, therefore, should be consumed in sufficient quantities by women of child-bearing age.

35

Preventive measures are probably the most effective method of dealing with these conditions and such measures should include diet and dietary supplementation. Although the etiology of disease is multi-factorial, 5 certain dietary supplements have been shown to provide a statistically significant benefit in reducing the risk or reducing the incidence of various diseases and conditions. However, to date, the approach to micronutrient supplementation has not considered the 10 changing needs of adult women. A more individualized, sophisticated, and targeted approach is clearly necessary. Because the incidence of these conditions varies with the different life stages of a woman, there is a need for dietary supplementation targeted to these 15 changing health risks at each of the life stages.

20

#### SUMMARY OF THE INVENTION

In one aspect of the present invention there are provided dietary supplements for supplementing the dietary needs of women and preventing or reducing life stage associated health risks during each of their 25 principal adult life stages (pre-perimenopause, perimenopause and menopause, or post-menopause).

In one embodiment of this aspect of the invention there is provided a dietary supplement for supplementing 30 the micronutrient and phytochemical needs of pre-perimenopausal women to prevent or reduce the risk of fetal neural tube defects, iron deficiency anemia, PMS, osteoporosis, coronary heart disease, cervical dysplasia and some cancers throughout that stage and the rest of a 35 woman's life, comprising about 200 to about 500 mg

calcium, about 100 to about 200 mg magnesium, about 0.5 to about 1.5 mg boron, about 0.5 to about 1.5 mg copper, about 2 to about 2.6 mg manganese, about 10 to about 13 mg zinc, about 200 to about 300 IU vitamin D, about 12 to about 18 mg iron, about 400 to about 440  $\mu$ g folic acid, about 2 to about 10  $\mu$ g vitamin B<sub>12</sub>, about 50 to about 100 mg vitamin B<sub>6</sub>, about 50 to about 100  $\mu$ g chromium, about 100 to about 200 IU vitamin E, about 100 to about 1000 mg vitamin C and about 8 to less than 50 mg phytoestrogen in admixture with a biologically acceptable carrier.

In another embodiment of this aspect of the invention the dietary supplement is formulated to supplement the changing nutritional needs of perimenopausal and menopausal women for the prevention or reduction of the risk of PMS, symptoms of menopause, fetal neural tube defects, osteoporosis, CHD, cervical dysplasia and some forms of cancer throughout that stage and the rest of a woman's life. This dietary supplement comprises from about 200 to about 1000 mg calcium; from about 100 to about 200 mg magnesium; from about 1.5 to about 2.5 mg boron; from about 1.5 to about 2.5 mg copper; from about 2.4 to about 3.6 mg manganese; from about 12 to about 15 mg zinc; from about 300 to about 400 IU vitamin D; from about 10 to about 15 mg iron; from about 400 to about 440  $\mu$ g folic acid; from about 2 to about 15  $\mu$ g vitamin B<sub>12</sub>; from about 50 to about 100 mg vitamin B<sub>6</sub>; from about 75 to about 200  $\mu$ g chromium; from about 200 to about 400 IU vitamin E; from about 200 to about 1000 mg vitamin C; and from about 10 to less than 50 mg phytoestrogen in admixture with a biologically acceptable carrier.

In yet another embodiment of this aspect of the

invention the dietary supplement is formulated to supplement the increased nutritional needs of post-menopausal women for the prevention or reduction of the risk of coronary heart disease, some forms of cancer and osteoporosis throughout the final stage of her life. This dietary supplement comprises about 200 to about 1500 mg calcium, about 150 to about 250 mg magnesium, about 2.5 to about 3.5 mg boron, about 2.5 to about 3.5 mg copper, about 4.4 to about 5.6 mg manganese, about 15 to about 18 mg zinc, about 300 to about 800 IU vitamin D, about 5 to about 10 mg iron, about 400 to about 440  $\mu$ g folic acid, about 2 to about 18  $\mu$ g vitamin B<sub>12</sub>, about 1.6 to about 10 mg vitamin B<sub>6</sub>, about 100 to about 200  $\mu$ g chromium, about 350 to about 800 IU vitamin E, about 300 to about 1000 mg vitamin C and about 10 to less than 50 mg phytoestrogen in admixture with a biologically acceptable carrier.

The dietary supplements of this invention may be formulated as a tablet, capsule, powder, gel or liquid, or dietary bar and are preferably formulated for once daily administration. They may be provided as a series or as individual compositions.

In another aspect of the invention, there is provided a method for supplementing the dietary needs and preventing or reducing life stage associated health risks in pre-perimenopausal women, perimenopausal and menopausal women, and/or post-menopausal women. This method comprises the administration to the woman of an effective amount of the life stage appropriate dietary supplement of the invention throughout that life stage. Preferably, a life stage appropriate dietary supplement of the invention is administered throughout each of the



three principal adult life stages of the woman.

Unexpectedly, the compositions of the present invention provide women with physiologically effective phytoestrogen even when phytoestrogens are administered at levels of less than 25 mg per day, preferably at levels of less than 20 mg per day. As such, it is another advantage of this invention to provide compositions and methods for supplementing women's micronutrient needs by providing phytoestrogens at these levels.

In another aspect of the invention there is provided a once daily dietary supplement formulated specifically for the nutritional needs of peri-menopausal and menopausal women. This dietary supplement comprises less than about 20 mg phytoestrogen, preferably less than about 15 mg, and most preferably about 14.5 mg to about 1 mg phytoestrogen once a day in admixture with a biologically acceptable carrier.

There is further provided a method of supplementing the dietary needs of peri-menopausal and menopausal women. This method comprises administering a composition comprising less than 20 mg phytoestrogen, preferably less than about 15 mg and most preferably from less than about 14.5 mg to about 1 mg phytoestrogen once per day to a woman in need thereof in admixture with a biologically acceptable carrier.

30

#### DETAILED DESCRIPTION OF THE INVENTION

The present invention provides dietary supplements for women that are designed to meet a woman's health needs at each particular stage of her life, such as pre-

perimenopause, perimenopause and menopause, or post-menopause, or during transition from one such life cycle into the next. This is accomplished by supplying, in the dietary supplements of the invention, a variety of  
5 nutrients that address common health risks associated with each of these life stages. Thus, each of the dietary supplements of the present invention provides a variety of nutrients, including antioxidants to increase the resistance of LDL cholesterol to oxidation, elements  
10 to enhance calcium absorption and utilization, nutrients to address iron deficiency anemia, folic acid to prevent fetal neural tube defects, compounds to reduce serum homocysteine and improve the lipid profile and phytoestrogens to reduce the symptoms of menopause, as  
15 well as to help in the prevention of osteoporosis, breast cancer and CHD. Furthermore, the amount of each nutrient present varies according to the life stage for which the composition is targeted.

20 The life stage specific dietary supplements of this invention are not meant to replace a well-balanced diet, but are instead intended to supplement a prudent diet. Unlike known broad-based dietary supplements, this invention does not merely provide the prescribed  
25 Recommended Daily Allowance (RDA) of micronutrients, but rather is geared to emphasize the disease prevention properties of micronutrient supplementation. Thus, cumulative beneficial and preventive effects should be achieved by dietary supplementation with the appropriate  
30 dietary supplement of the invention, especially when diligently used for more than one life stage.

As discussed above, a woman passes through three principal adult life stages. The onset of each of the  
35 various lifestages can occur at different ages for

different individuals and the ages suggested below for the various lifestages are only approximations. The pre-perimenopause life stage (Stage I), approximately ages 18 to 45, includes the child-bearing or reproductive life stage, which is a period of maximum ovarian function. Major health concerns that arise during this life stage include iron deficiency anemia, PMS and prevention of neural tube defects during pregnancy.

The perimenopause and menopause stage (Stage II), approximately ages 45 to 55, is characterized by decreasing ovarian function. At first, menstrual cycles may be erratic and PMS may intensify. For 80% of all women this stage will eventually include symptoms of the menopause, such as hot flashes, night sweats, insomnia, fatigue, and mood swings. The rate of bone loss accelerates and the lipid profile becomes more atherogenic, thus setting the stage for the future onset of CHD and osteoporosis.

The final stage, post-menopause (Stage III), age 55 plus, is characterized by complete cessation of ovarian function and an increase in the incidence of cancer, osteoporotic fracture and CHD. Menstrual related anemia, PMS and pregnancy are no longer health concerns during this life stage.

The dietary supplements of this invention contain vitamins, minerals and other compounds that are specifically included to address common health concerns that arise during each of these life stages. Moreover, they are formulated to prevent or lessen the risk of conditions known to develop in later life stages. For example, the dietary supplement intended for use during pre-perimenopause (Stage I dietary supplement) contains

compounds to counter the risk of fetal neural tube defects, lessen or prevent PMS and iron deficiency anemia and prevent or lessen the risk of osteoporosis, coronary heart disease and cancer, which are generally manifest in the post-menopause life stage.

Phytoestrogens are included in each of the dietary supplements of this invention. These compounds have been demonstrated by clinical trials to modulate the menstrual cycle, reduce menopausal symptoms, and lower LDL cholesterol levels. J. Nutr., 1996, 126(1): 161-7; N. Engl. J. Med., 1995, 333: 276-82. Epidemiologic observations indicate women in countries where diets are rich in phytoestrogen (averaging about 40-50 mg/day) have a decreased incidence of breast cancer, menopausal symptoms and osteoporosis. Nutr. Cancer, 1994, 21:113-131; J. Nutr., 1995, 125: 757S-770S; Am. J. Clin. Nutr. 1995, 62:645. Animal studies have provided a biological basis for these observations. J. Ster. Biochem & Mol. Bio., 1992, 41(3-8): 331-7; First International Symposium on the role of Soy and Preventing and Treating Chronic Disease (1994), Speaker Abstracts.

In particular, with respect to alleviating menopausal symptoms, the use of moderate to high levels, i.e., generally from at least 20 to 90 mg per day of phytoestrogens, to reduce the symptoms of menopause is known in the art. Some researchers believe that a diet having such moderate to high levels of phytoestrogens may play a role in reducing the incidence of distressful symptoms of menopause; others believe that phytoestrogens alone are inadequate without adjunctive therapy. Adlercruetz, et al. INPHARMA (1996), *Examining the Benefits of Dietary Phytoestrogens*; Adlercruetz, et al., The Lancet (1992), 339:1233. Id. U.S. Patent

5,498,631 discloses that moderate to high levels of isoflavonoids effectively reduce the symptoms of conditions caused by altered levels of estrogen such as menopause and premenstrual syndrome. Solgar, a New Jersey company, provides a pill called "Genistein" formulated from soy isoflavone extract containing 15 to 20 mg of a mixture of genestein and daidzein for twice daily consumption, which would provide at least 30 to 40 mg phytoestrogen per day.

10

Phytoestrogens are a class of isoflavones or isoflavonoids derived from plants, commonly soy beans. The plant source, however, is not critical. Some phytoestrogens, such as genistin, glycitin and diadzin contain a glycosidic moiety, whereas other phytoestrogens are nonglycosylated, e.g., genistein, glycitein and daidzein. Phytoestrogens obtained from a single plant generally are a mixture of both glycosylated and nonglycosylated forms. The present dietary supplements generally contain a mixture of phytoestrogens; however, purified phytoestrogens may be used. Mixtures of phytoestrogen may be obtained commercially. Phytoestrogen levels of less than 25 mg per day, preferably greater than 5 to about 25 mg per day, and most preferably about 10 to about 20 mg per day, provide women with phytoestrogen levels that are physiologically effective and may be used to supplement women's micronutrient needs.

30

Vitamin B<sub>12</sub>, vitamin B<sub>6</sub> and folic acid are included in each of the life stage specific dietary supplements of this invention. These elements act synergistically to reduce serum homocysteine, high levels of which are associated with coronary heart disease. Am. J. Clin.

Nutr., 1992, 55:131-138; New Eng. J. Med., 1992, 32:1832-1835; Am J. Clin. Nutr., 1989, 50:353-358. The amount of folic acid in the three dietary supplements of this invention is maintained at about the same level in all  
5 three compositions, since folic acid not only reduces the risk of fetal neural tube defects, but, as noted above, also has been shown to have beneficial cardiac effects and to decrease the risk of cervical dysplasia. Scand. J. Clin. Lab Invest., 1988, 48:215-221. On the other  
10 hand, larger doses of vitamin B<sub>6</sub> are included in the Stage I and Stage II formulations, as compared to Stage III, to assist in alleviating PMS symptoms. J. Royal Coll. Gen. Prac., 1989, 39:364-368; Obstetrics and Gyn., 1987, 70:147-149.

15

Other components of the dietary supplements of this invention include vitamin D, calcium, magnesium, manganese, copper, zinc, boron and chromium. The combination of vitamin D, and magnesium, manganese,  
20 copper, zinc, and boron (the "enhancement compounds") acts synergistically with calcium to improve calcium absorption and/or utilization and thereby enhance bone density. Am. J. Clin. Nutr., 1982, 36:1046-1059; J. Am Col. Nutr., 1993, 12:383-389; Magnesium Trace Elem.,  
25 1990, 9:61-69; Am. J. Clin. Nutr., 1991, 54:177S-226S; Clin. Obstetrics and Gyn., 1987, 30:789-811. Chromium is included to optimize glucose and lipid metabolism. Diabetes Care, 1994, 17:1449-1452; Metabolism, 1992, 41:768-771; Biol. Trace Element Res., 1992, 32:19-24.

30

Aging is associated with an increased production of oxygen free radicals (highly toxic molecules) which contribute to the pathogenesis of many chronic diseases. This invention is formulated to address this issue.  
35 Thus, antioxidants, such as vitamin E, are included

particularly to reduce atherogenicity of LDL cholesterol particles which reduces damage to arterial walls. Am. J. Clin. Nutr., 1991, 53:305S-313S; Lancet, 1996, 347:781-786. Another antioxidant, Vitamin C, is included to  
5 lower the risk of breast and other cancers. Vitamin E and Vitamin C may work together in a synergistic fashion. Am. J. Clin. Nutr. 1991, 54: 1310S-1314S.

Each of the life stage dietary supplements of this  
10 invention are formulated specifically to contain an amount of each of the above-discussed components sufficient to prevent or reduce health risks associated with Stage I, Stage II or Stage III of a woman's life.

15 The dose of iron is highest in the Stage I dietary supplement of this invention and lowest in the Stage III dietary supplement, because iron deficiency anemia is a major health concern of menstruating women (Stage I and part of Stage II). Vitamin B<sub>12</sub> deficiency results in  
20 pernicious anemia. Because this condition can be clinically masked if folate is provided in the diet without vitamin B<sub>12</sub>, all formulations of this invention contain both folic acid and Vitamin B<sub>12</sub>.

25 Stage I compositions also contain an amount of vitamin B<sub>6</sub> sufficient to reduce symptoms of PMS and to compensate for reduced levels of this vitamin caused by oral contraceptive use. The amount of folic acid contained in the Stage I nutritional supplement is  
30 sufficient to prevent fetal neural tube defects during pregnancy, as well as to reduce the risk of cardiovascular disease by maintaining low homocysteine levels. It also reduces the risk of cervical dysplasia.

35 Thus, the Stage I dietary supplement contains an

amount of vitamin B<sub>6</sub> sufficient to reduce the effects of PMS, an amount of folic acid sufficient to prevent fetal neural tube defects and provide cardiac benefit, a sufficient amount of vitamin B<sub>12</sub> to act in concert with vitamin B<sub>6</sub> and folic acid present in the composition to reduce the levels of serum homocysteine, a sufficient amount of chromium to enhance glucose and lipid metabolism, antioxidants to help prevent CHD and some cancers, and calcium, together with a combination of other nutrients known to enhance its absorption and/or utilization to prevent osteoporosis, and an amount of phytoestrogens to beneficially modulate menses and provide protection against osteoporosis, some cancers and CHD. The Stage I dietary supplement is therefore particularly suited to meet the needs and address the health risks of a young adult female, while also lessening the risk of osteoporosis, cancer and coronary heart disease occurring in later life.

The dietary supplements formulated for the perimenopause and menopause lifestage (Stage II composition) include a higher dosage of phytoestrogens than used in the dietary supplement for the pre-perimenopausal lifestage because phytoestrogens reduce menopausal symptoms, and to provide even more protection against osteoporosis, cancer and CHD, the incidence of all of which increases with age. Similarly, components that affect calcium uptake and utilization are also increased in the Stage II dietary supplement since the amount of bone loss increases with menopause.

Concomitant with the onset of the menopause is a worsening of the lipid profile. LDL-cholesterol and total cholesterol increase significantly, while HDL-cholesterol decreases. To address this problem, the



levels of both phytoestrogens and chromium have been increased in the Stage II composition relative to the Stage I composition. Antioxidant levels have also been increased to help prevent the age-related onset of CHD and breast cancer.

The Stage III dietary supplement of this invention is formulated to address the health concerns and health risks that occur with greater frequency in the post-menopausal years, e.g., osteoporosis, cancer and coronary heart disease. Stage III compositions contain phytoestrogen in the same concentration as Stage II. However, calcium, vitamin D, and the enhancement compounds are increased, as are the antioxidants and chromium. Chromium has a positive effect on blood sugar levels and the lipid profile. On the other hand, the levels of vitamin B<sub>6</sub> and iron are decreased, because the health concerns addressed by higher amounts of these components are of less relevance.

20

Optionally, the dietary supplements of this invention may further contain an amount of vitamin A or mixed carotenoids sufficient to supplement the nutritional needs of a woman at a particular lifestage. Vitamin A may be provided as preformed vitamin A or as mixed carotenoids, or both. There are more than 500 naturally occurring carotenoids, about 50 of which can serve as precursors of retinol and therefore have provitamin A activity. These include alpha- and beta-carotene and cryptoxanthin. However, non provitamin A carotenoids, such as lutein and lycopene have also been shown to have beneficial effects and may also be provided. Lycopene intake, for example, has been inversely associated with the risk of cervical cancer. Nutr & Cancer 1994, 21:193-201; Internat J. Cancer 1991;

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48:34-8.

The amount of preformed vitamin A and mixed carotenoids included in the Stage I dietary supplement is in the range of about 400 to about 1200 RE, preferably about 600 to about 1000 RE, and most preferably about 800 RE. The amount of preformed vitamin A and mixed carotenoids included in the Stage II dietary supplement is in the range of about 800 to about 1600 RE, preferably about 1000 to about 1400 RE, and most preferably about 1200 RE. The amount of preformed vitamin A and mixed carotenoids included in the Stage III dietary supplement is in the range of about 1200 to about 2000 RE, preferably about 1400 to about 1800 RE, and most preferably about 1600 RE. Preferably, the amount of preformed vitamin A is about 200 to about 400 RE, and most preferably about 400 RE.

Each of the dietary supplements of this invention is formulated to prevent and reduce the risk of disease during one of three specific life stages, during the transition from one life stage to the next, and during later stages of life. Administration of the dietary supplements of this invention during the appropriate life stage reduces the risk factors for disease, such as iron deficiency anemia during the pre-perimenopausal life stage, high cholesterol during the perimenopausal and menopausal life stage, and CHD, osteoporosis, and some cancers during the post-menopausal life stage.

Maximum benefit is obtained by supplementation of the diet with the life stage appropriate dietary supplement throughout the entire life cycle; however, benefit is also obtained when supplementation is begun at any time during a particular life cycle.

For example, supplementation of the diet with the Stage I dietary supplement at age 30 to 40, which is well into the pre-perimenopausal life stage, lowers the risk of, or prevents, future osteoporosis, cancer and coronary heart disease, and provides health benefits to those conditions that present during this life cycle, e.g., PMS, fetal neural tube defects, and iron deficiency anemia. It is understood that the phrase "administration throughout the life cycle", as used herein, means continual administration from any time during a life cycle that supplementation is begun.

The dietary supplements of the present invention may be formulated using any pharmaceutically acceptable forms of the vitamins, minerals and other nutrients discussed above, including their salts. Preferred forms are calcium carbonate, magnesium hydroxide or magnesium sulfate, sodium tetraborate, cupric oxide, manganese sulfate, zinc sulfate, cholecalciferol, ferrous fumarate, pyridoxine hydrochloride, chromium picolinate, d-alpha-tocopherol acetate, and ascorbic acid. They may be formulated into capsules, tablets, powders, gels or liquids. The dietary supplements may be formulated as powders, for example, for mixing with consumable liquids such as milk, juice, water or consumable gels or syrups for mixing into other dietary liquids or foods. The dietary supplements of this invention may be formulated with other foods or liquids to provide premeasured supplemental foods, such as single serving bars, for example. Flavorings, binders, protein, complex carbohydrates, and the like may be added as needed.

The dietary supplements of the invention are intended for daily administration. Preferably, they are formulated for once-daily administration, but may be

formulated in multiple portions or as time release compositions for more or less frequent administration; for example, the dietary supplement may be formulated as two tablets for twice daily administration, or as a  
5 sustained release capsule for administration every three days. In the latter instance, the capsule is formulated to release the daily amount of nutrients prescribed by the dietary supplements of the invention during each of the three days. For reasons of size (ease of swallowing)  
10 or improved bioabsorption or utilization (e.g., before or after a meal or before sleep), a given dosage may be divided into two, three, or more tablets (or capsules, etc.). A daily dosage may be administered as one tablet, as two tablets taken together, or as two tablets taken  
15 separately (e.g., one in the morning and one in the evening).

Specific formulation for each of the three lifestage specific dietary supplements is provided below.

20

#### STAGE I DIETARY SUPPLEMENT

The dietary supplement for pre-perimenopausal women includes from about 200 to about 500 mg calcium, preferably from about 200 to about 300 mg calcium, and  
25 most preferably about 200 mg calcium; from about 100 to about 200 mg magnesium, preferably from about 100 to about 150 mg magnesium, and most preferably about 100 mg magnesium; from about 0.5 to about 1.5 mg boron, preferably about 0.7 to about 1.3 mg boron, and most  
30 preferably about 1 mg boron; from about 0.5 to about 1.5 mg copper, preferably about 0.7 to about 1.3 mg copper, and most preferably about 1 mg copper; from about 2 to about 2.6 mg manganese, preferably about 2 to about 2.4 mg manganese, and most preferably about 2 mg manganese;  
35 from about 10 to about 13 mg zinc, preferably about 10 to

about 12 mg zinc, and most preferably about 10 mg zinc;  
from about 200 to about 300 IU vitamin D, preferably  
about 200 to about 250 IU vitamin D, and most preferably  
about 200 IU vitamin D; from about 12 to about 18 mg  
5 iron, preferably about 16 to about 18 mg iron, and most  
preferably about 18 mg iron; from about 400 to about 440  
 $\mu\text{g}$  folic acid, preferably about 400 to about 420  $\mu\text{g}$  folic  
acid, and most preferably about 400  $\mu\text{g}$  folic acid; from  
about 2 to about 10  $\mu\text{g}$  vitamin B<sub>12</sub>, preferably about 2 to  
10 about 4  $\mu\text{g}$  vitamin B<sub>12</sub>, and most preferably about 2  $\mu\text{g}$   
vitamin B<sub>12</sub>; from about 50 to about 100 mg vitamin B<sub>6</sub>,  
preferably about 50 to about 65 mg vitamin B<sub>6</sub>, and most  
preferably about 50 mg vitamin B<sub>6</sub>; from about 50 to about  
100  $\mu\text{g}$  chromium, preferably about 50 to about 75  $\mu\text{g}$   
15 chromium, and most preferably about 50  $\mu\text{g}$  chromium; from  
about 100 to about 200 IU vitamin E, preferably about 100  
to about 150 IU vitamin E, and most preferably about 100  
IU vitamin E; from about 100 to about 1000 mg vitamin C,  
preferably about 100 to about 150 mg vitamin C, and most  
20 preferably about 100 mg vitamin C; and from about 8 to  
less than 50 mg phytoestrogen, preferably about 8 to  
about 12 mg phytoestrogen, and most preferably about 10  
mg phytoestrogen.

25 This range of folic acid has been shown to be  
effective in preventing fetal neural tube defects and  
reducing the risk of cervical dysplasia; the amount of  
vitamin B<sub>6</sub> is sufficient to reduce at least some symptoms  
of PMS; the amounts of vitamin B<sub>12</sub>, vitamin B<sub>6</sub> and folic  
30 acid have been shown to reduce serum homocysteine; the  
amount of iron present in the composition is sufficient  
to reduce or prevent iron deficiency anemia; and  
phytoestrogen, antioxidants and chromium help reduce the  
risk of cardiovascular disease. Antioxidants and  
35 phytoestrogens also provide some protection against

osteoporosis and some cancers.

A preferred Stage I daily dietary supplement is shown in Table I.

5

STAGE II DIETARY SUPPLEMENT

The dietary supplement for perimenopausal and menopausal women includes from about 200 to about 1000 mg calcium, preferably from about 300 to about 400 mg calcium, and most preferably about 300 mg calcium; from about 100 to about 200 mg magnesium, preferably from about 100 to about 150 mg magnesium, and most preferably about 150 mg magnesium; from about 1.5 to about 2.5 mg boron, preferably about 1.7 to about 2.3 mg boron, and most preferably about 2 mg boron; from about 1.5 to about 2.5 mg copper, preferably about 1.7 to about 2.3 mg copper, and most preferably about 2 mg copper; from about 2.4 to about 3.6 mg manganese, preferably about 2.6 to about 3.4 mg manganese, and most preferably about 3 mg manganese; from about 12 to about 15 mg zinc, preferably about 12 to about 14 mg zinc, and most preferably about 12 mg zinc; from about 300 to about 400 IU vitamin D, preferably about 300 to about 350 IU vitamin D, and most preferably about 300 IU vitamin D; from about 10 to about 15 mg iron, preferably about 13 to 15 mg iron, and most preferably about 15 mg iron; from about 400 to about 440  $\mu$ g folic acid, preferably about 400 to about 420  $\mu$ g folic acid, and most preferably about 400  $\mu$ g folic acid; from about 2 to about 15  $\mu$ g vitamin B<sub>12</sub>, preferably about 2 to about 6  $\mu$ g vitamin B<sub>12</sub>, and most preferably about 2  $\mu$ g B<sub>12</sub>, from about 50 to about 100 mg vitamin B<sub>6</sub>, preferably about 50 to about 65 mg vitamin B<sub>6</sub>, and most preferably about 50 mg vitamin B<sub>6</sub>; from about 75 to about 200  $\mu$ g chromium, preferably about 75 to about 100  $\mu$ g chromium, and most preferably about 75  $\mu$ g chromium; from about 200 to about

35

400 IU vitamin E, preferably about 200 to about 300 IU vitamin E, and most preferably about 200 IU vitamin E; from about 200 to about 1000 mg vitamin C, preferably about 200 to about 300 mg vitamin C, and most preferably about 200 mg Vitamin C; and from about 10 to less than 50 mg phytoestrogen, preferably about 12 to about 17 mg phytoestrogen, and most preferably 15 mg phytoestrogen.

The amount of calcium, magnesium, boron, copper, manganese, zinc and vitamin D in the Stage II composition has been increased in comparison to the Stage I composition since these nutrients have been shown to enhance calcium absorption and/or utilization; the amount of vitamin B<sub>6</sub> is the same as in the Stage I composition and is sufficient to prevent or reduce symptoms of PMS; the amounts of folic acid will prevent fetal neural tube defects and reduce the risk of cervical dysplasia, and in combination with vitamin B<sub>12</sub> and vitamin B<sub>6</sub> is associated with a reduced risk of CHD; chromium has also been increased to help regulate the lipid profile and thereby reduce the risk of CHD; the amount of phytoestrogen contributes to the reduction of menopausal symptoms, osteoporosis, CHD and some forms of cancer, and therefore is increased in the composition for the second life stage. Similarly, the amount of antioxidants are increased in the Stage II composition because they also provide protection against CHD and some cancers.

A preferred Stage II daily dietary supplement is shown in Table I.

#### STAGE III DIETARY SUPPLEMENT

The dietary supplement for post-menopausal women includes from about 200 to about 1500 mg calcium,

preferably from about 300 to about 500 mg calcium, and most preferably about 400 mg calcium; from about 150 to about 250 mg magnesium, preferably from about 150 to about 200 mg magnesium, and most preferably about 200 mg magnesium; from about 2.5 to about 3.5 mg boron, preferably about 2.7 to about 3.3 mg boron, and most preferably about 3 mg boron; from about 2.5 to about 3.5 mg copper, preferably about 2.7 to about 3.3 mg copper, and most preferably about 3 mg copper; from about 4.4 to about 5.6 mg manganese, preferably about 4.6 to about 5.4 mg manganese, and most preferably about 5.0 mg manganese; from about 15 to about 18 mg zinc, preferably about 15 to about 17 mg zinc, and most preferably about 15 mg zinc; from about 300 to about 800 IU vitamin D, preferably about 350 to about 400 IU vitamin D, and most preferably about 400 IU vitamin D; from about 5 to about 10 mg iron, preferably about 8 to 10 mg iron, and most preferably about 10 mg iron; from about 400 to about 440  $\mu$ g folic acid, preferably about 400 to about 420  $\mu$ g folic acid, and most preferably about 400  $\mu$ g folic acid; from about 2 to about 18  $\mu$ g vitamin B<sub>12</sub>, preferably about 2 to about 8  $\mu$ g vitamin B<sub>12</sub>, and most preferably about 2  $\mu$ g vitamin B<sub>12</sub>; from about 1.6 to about 10 mg vitamin B<sub>6</sub>, preferably about 1.6 to 3.2 mg vitamin B<sub>6</sub>, most preferably about 1.6 mg vitamin B<sub>6</sub>; from about 100 to about 200  $\mu$ g chromium, preferably about 100 to about 150  $\mu$ g chromium, and most preferably about 100  $\mu$ g chromium; from about 350 to about 800 IU vitamin E, preferably about 350 to about 450 IU vitamin E, and most preferably about 400 IU vitamin E; from about 300 to about 1000 mg vitamin C, preferably about 350 to about 450 mg vitamin C, and most preferably about 400 mg vitamin C; and from about 10 to less than 50 mg phytoestrogen, preferably about 12 to about 17 mg phytoestrogen, and most preferably about 15 mg phytoestrogen.



The amounts of calcium, manganese, boron, copper, magnesium, zinc and vitamin D are optimized to enhance calcium uptake and/or utilization for the prevention of osteoporotic fractures; the amounts of antioxidant, vitamin B<sub>12</sub>, vitamin B<sub>6</sub>, folic acid, and chromium are maximized to prevent or reduce the risk of CHD; phytoestrogens and antioxidants contribute to reducing the risk of cardiovascular disease and some cancers.

A preferred Stage III daily dietary supplement is shown in Table I.

**TABLE I**  
**DIETARY SUPPLEMENTS**

COMPONENT	STAGE I	STAGE II	STAGE III
Calcium	200 mg	300 mg	400 mg
Magnesium	100 mg	150 mg	200 mg
Boron	1 mg	2 mg	3 mg
Copper	1 mg	2 mg	3 mg
Manganese	2 mg	3 mg	5 mg
Zinc	10 mg	12 mg	15 mg
Vitamin D	200 IU	300 IU	400 IU
Iron	18 mg	15 mg	10 mg
Folic Acid	400 µg	400 µg	400 µg
Vitamin B <sub>12</sub>	2 µg	2 µg	2 µg
Vitamin B <sub>6</sub>	50 mg	50 mg	1.6 mg
Chromium	50 µg	75 µg	100 µg
Vitamin E	100 IU	200 IU	400 IU
Vitamin C	100 mg	200 mg	400 mg
Phytoestrogen	10 mg	15 mg	15 mg

In a second aspect of the invention there is

provided a method for preventing or lessening the risk of life stage associated diseases and health conditions in women by orally administering a dietary supplement of this invention during the appropriate life stage of the woman. For example, the Stage I dietary supplement of this invention is orally administered to a pre-perimenopausal woman, the Stage II dietary supplement is orally administered to the woman when she reaches the perimenopausal and menopausal stage and the Stage III dietary supplement of this invention is administered to the woman when she reaches the post-menopausal stage. In a preferred embodiment, the appropriate dietary supplement is administered throughout at least one life stage of the woman, most preferably throughout the three adult life stages defined herein.

Although approximate age ranges for these stages are noted above, any individual woman may have an accelerated course through these phases. Delayed transitions can also occur but are less likely. Thus, a woman taking the Stage I formulation who begins to experience hot flashes, insomnia, or other menopausal symptoms would benefit more from the Stage II formulation and should switch to that formulation at whatever age those symptoms occur. It is suggested that she remain on the Stage II formulation until she is clearly post-menopausal as determined by medical convention (generally an increased FSH --follicle stimulating hormone-- and no menstrual cycle for twelve months). The Stage III formulation is then recommended.

30

Similarly, when a woman has had cessation of menses related to decreased ovarian function as determined by medical convention, she should switch from the Stage I to the Stage II formulation for at least six months to one year, even though she has had no distressing menopausal

35

symptoms. When clearly through this transition phase, the Stage III formulation is recommended due to its additional preventive properties for post-menopausal diseases.

5

And, a woman who undergoes surgical menopause at an early age, e.g., at 35 years, no longer requires the Stage I formulation. While the Stage II composition would not be inappropriate for a year or two, the preferred formulation for this woman would be the Stage III formulation because she has gone from a child-bearing phase to a post-menopausal phase without a significant transition period.

15 The present method for preventing or lessening the risk of life stage associated health conditions is effective in the prevention of fetal neural tube defects, prevention or reduction of symptoms of PMS and menopause, prevention or reduction of the risk of developing  
20 osteoporosis, iron deficiency anemia, coronary heart disease, some cancers and cervical dysplasia.

In another aspect of the invention, there is provided a dietary supplement formulated specifically for  
25 peri-menopausal and menopausal women. The supplement may also be used by pre-perimenopausal women to, for example, enhance the effects of supplementation once the peri-menopausal and menopausal life stage is reached, or by post-menopausal women exhibiting residual symptoms of  
30 menopause. Use during the pre-perimenopausal life stages may also aid in regulating or may otherwise positively impact the menstrual cycle.

The dietary supplement of this aspect of the

invention is a once daily supplement comprising physiologically effective phytoestrogen in an amount of less than about 20 mg, preferably less than about 15 mg and more preferably, less than about 14.5 mg to about 1  
5 mg.

The phytoestrogen to be used may be selected from concentrated naturally-occurring phytoestrogen (such as whole soybean extract), synthesized phytoestrogen, or  
10 mixtures thereof. One or more different phytoestrogens may be included. Preferably, the phytoestrogen is selected from the group consisting of genistin, glycitin, daidzin, malonyl daidzin, malonyl genistin, malonyl glycitin, acetyl glycitin, acetyl daidzin, acetyl  
15 genistin, genistein, glycitein, daidzein and mixtures thereof.

The phytoestrogen may be derived from any suitable source, for example, from a plant extract rich in  
20 phytoestrogens. Preferably, the phytoestrogen is derived from whole soybean (as opposed to soy germ). Other sources of phytoestrogen however may be utilized. The phytoestrogens may be glycosylated, such as genistin, glycitin or daidzin, malonyl daidzin, malonyl genistin,  
25 malonyl glycitin, acetyl glycitin, acetyl daidzin, acetyl genistin, or non-glycosylated, such as genistein, glycitein or daidzein. Preferably, the phytoestrogen has the following phytoestrogen profile (by weight percent):  
30 about 31 to 35% daidzin, about 8 to 10% glycitin, about 36 to 40% genistin, about 3 to 5% malonyl daidzin, about 0.5 to 2.5% malonyl glycitin, about 2.6 to 4.6% malonyl genistin, about 3.7 to 5.7% acetyl daidzin, about 0.1 to 1.1% acetyl glycitin, about 3.2 to 5.2% acetyl genistin,

about 0.1 to 1% daidzein, about 0.1 to 1% glycitein, and about 0.1 to 0.9% genistein. Most preferably the phytoestrogen has a phytoestrogen profile similar to that described in Table II, which sets forth the phytoestrogen profile for total phytoestrogens in a phytoestrogen concentrate derived from whole soybean.

The dietary supplement may be provided in tablet, patch, gel, cream or capsule form, for example or formulated in a palatable confection such as a confectionary bar, beverage, cereal, powder, chewing gum and the like.

In a preferred embodiment, there is provided a once daily dietary supplement containing a mixture of daidzin, glycitin, genistin, malonyl daidzin, malonyl genistin, malonyl glycitin, acetyl glycitin, acetyl daidzin, acetyl genistin, genistein, glycitein and daidzein in a total weight amount of about 10 to about 15 mg, more preferably 13 to 15 mg. Preferably, each of the phytoestrogens is provided in the following percentages (by weight) of the total phytoestrogens: about 33% daidzin, about 9% glycitin, about 38% genistin, about 4% malonyl daidzin, about 1.5% malonyl glycitin, about 3.6% malonyl genistin, about 4.7% acetyl daidzin, about 0.6% acetyl glycitin, about 4.2% acetyl genistin, about 0.5% daidzein, about 0.5% glycitein, and about 0.4% genistein.

In a most preferred embodiment, a supplement is provided using about 50 mg of soybean phytoestrogen concentrate having the phytoestrogen profile set forth in Table II, to give a phytoestrogen content of 14.15. This tablet provides phytoestrogens in the following forms and

amounts: about 4.726 mg daidzin, about 1.257 mg  
 glycitin, about 5.312 mg genistin, about 0.586 mg malonyl  
 daidzin, about 0.217 mg malonyl glycitin, about 0.510 mg  
 malonyl genistin, about 0.670 mg acetyl daidzin, about  
 5 0.082 mg acetyl glycitin, about 0.595 mg acetyl genistin,  
 about 0.076 mg daidzein, about 0.062 mg glycitein, and  
 about .060 mg genistein (See Table II).

10 **TABLE II**  
**PHYTOESTROGEN SUPPLEMENT**

PHYTOESTROGEN	wt%	mg/50 g of whole soybean phytoestrogen concentrate	ppm ( $\mu\text{g/g}$ ) in whole soybean phytoestrogen concentrate
Daidzin	33	4.726	94527
Glycitin	9	1.257	25144
15 Genistin	38	5.312	106239
Malonyl Daidzin	4	0.586	11721
Malonyl Glycitin	1.5	0.217	4341
Malonyl Genistin	3.6	0.510	10200
Acetyl Daidzin	4.7	0.670	13390
20 Acetyl Glycitin	0.6	0.082	1633
Acetyl Genistin	4.2	0.595	11907
Daidzein	0.5	0.076	1510
Glycitein	0.5	0.062	1243
Genistein	0.4	0.060	1192
25 TOTAL	100	14.15	283047

30 **EXAMPLE 1**

The diet of a pre-perimenopausal woman is

supplemented daily with the Stage I dietary supplement of this invention. The dietary supplement is administered in tablet form formulated for once daily administration. Supplementation of the diet is carried out throughout the entire pre-perimenopausal life stage.

When the woman reaches the perimenopausal life stage, dietary supplementation is changed from the Stage I to Stage II dietary supplement of the invention. The Stage II dietary supplement is administered in the same manner as is the Stage I supplement. Dietary supplementation continues throughout perimenopause and menopause, after which the Stage III dietary supplement is administered in place of the Stage II supplement.

#### EXAMPLE 2

The diet of two menopausal women who were unable or unwilling to take hormonal replacement therapy (HRT) and who presented with menopausal symptoms including hot flashes, insomnia and night sweats that were marked to severe in quantity and/or quality was supplemented with a dietary regimen of about 15 mg/day phytoestrogen. Both women had been on HRT in the past (one woman for two and one half months and the other for two years). However, neither woman would consider its continued use. Both women had also tried alternative treatment regimens, such as acupuncture and Chinese herbs with little or no lasting relief.

Both women reported immediate relief (within several days) upon taking tablets containing about 15 mg/day of phytoestrogen. The effect got progressively better for four to six weeks at which time a plateau was reached.

Each woman reported a significant reduction in hot flashes, i.e., from more than twenty per day to less than five per day, as well as a reduction in their intensity (from "hot" to "warm flushes"). Night sweats  
5 were also significantly reduced and both the duration and quality of sleep improved.

A SMAC-18 laboratory analysis was obtained for each woman prior to the start of phytoestrogen therapy and  
10 again at four to six weeks and at eight to thirteen weeks after onset of phytoestrogen therapy. There were no adverse changes in the SMAC-18 data. Specifically, kidney function and liver enzyme levels remained  
unchanged.

15

As a comparison, at least one of the women was provided with a phytoestrogen supplement already on the market to substitute for the phytoestrogen supplement of the invention. She reported that it was completely  
unsatisfactory.



## WHAT IS CLAIMED IS:

1        Claim 1. A dietary supplement for supplementing the  
2        nutritional needs of pre-perimenopausal women comprising  
3        about 200 to about 500 mg calcium, about 100 to about 200  
4        mg magnesium, about 0.5 to about 1.5 mg boron, about 0.5  
5        to about 1.5 mg copper, about 2 to about 2.6 mg  
6        manganese, about 10 to about 13 mg zinc, about 200 to  
7        about 300 IU vitamin D, about 12 to about 18 mg iron,  
8        about 400 to about 440  $\mu$ g folic acid, about 2 to about 10  
9         $\mu$ g vitamin B<sub>12</sub>, about 50 to about 100 mg vitamin B<sub>6</sub>, about  
10       50 to about 100  $\mu$ g chromium, about 100 to about 200 IU  
11       vitamin E, about 100 to about 1000 mg vitamin C and about  
12       8 to less than 50 mg phytoestrogen in admixture with a  
13       biologically acceptable carrier.

1        Claim 2. The dietary supplement of claim 1 which  
2        further comprises from about 400 to about 1200 RE  
3        preformed vitamin A and mixed carotenoids.

1        Claim 3. The dietary supplement of claim 1 wherein  
2        said supplement is formulated in tablet, powder, liquid,  
3        capsule or gel form, or dietary bar.

1        Claim 4. The dietary supplement of claim 1  
2        comprising about 200 to about 300 mg calcium, about 100  
3        to about 150 mg magnesium, about 0.7 to about 1.3 mg  
4        boron, about 0.7 to about 1.3 mg copper, about 2 to about  
5        2.4 mg manganese, about 10 to about 12 mg zinc, about 200  
6        to about 250 IU vitamin D, about 16 to about 18 mg iron,  
7        about 400 to about 420  $\mu$ g folic acid, about 2 to about 4  
8         $\mu$ g vitamin B<sub>12</sub>, about 50 to about 65 mg vitamin B<sub>6</sub>, about  
9        50 to about 75  $\mu$ g chromium, about 100 to about 150 IU  
10       vitamin E, about 100 to about 150 mg vitamin C and about  
11       8 to about 12 mg phytoestrogen in admixture with a

12 biologically acceptable carrier.

1 Claim 5. The dietary supplement of claim 1  
2 comprising about 200 mg calcium, about 100 mg magnesium,  
3 about 1 mg boron, about 1 mg copper, about 2 mg  
4 manganese, about 10 mg zinc, about 200 IU vitamin D,  
5 about 18 mg iron, about 400 µg folic acid, about 2 µg  
6 vitamin B<sub>12</sub>, about 50 mg vitamin B<sub>6</sub>, about 50 µg chromium,  
7 about 100 IU vitamin E, about 100 mg vitamin C and about  
8 10 mg phytoestrogen in admixture with a biologically  
9 acceptable carrier.

1 Claim 6. A dietary supplement for supplementing the  
2 nutritional needs of perimenopausal and menopausal women  
3 comprising from about 200 to about 1000 mg calcium; from  
4 about 100 to about 200 mg magnesium; from about 1.5 to  
5 about 2.5 mg boron; from about 1.5 to about 2.5 mg  
6 copper; from about 2.4 to about 3.6 mg manganese; from  
7 about 12 to about 15 mg zinc; from about 300 to about 400  
8 IU vitamin D; from about 10 to about 15 mg iron; from  
9 about 400 to about 440 µg folic acid; from about 2 to  
10 about 15 µg vitamin B<sub>12</sub>; from about 50 to about 100 mg  
11 vitamin B<sub>6</sub>; from about 75 to about 200 µg chromium; from  
12 about 200 to about 400 IU vitamin E; from about 200 to  
13 about 1000 mg vitamin C; and from about 10 to less than  
14 50 mg phytoestrogen in admixture with a biologically  
15 acceptable carrier.

1 Claim 7. The dietary supplement of claim 6 which  
2 further comprises from about 800 to about 1600 RE  
3 preformed vitamin A and mixed carotenoids.

1 Claim 8. The dietary supplement of claim 6 wherein  
2 said supplement is formulated in tablet, powder, liquid,

3 capsule or gel form, or dietary bar.

1        Claim 9. The dietary supplement of claim 6  
2 comprising from about 300 to about 400 mg calcium; from  
3 about 100 to about 150 mg magnesium; from about 1.7 to  
4 about 2.3 mg boron; from about 1.7 to about 2.3 mg  
5 copper; from about 2.6 to about 3.4 mg manganese; from  
6 about 12 to about 14 mg zinc; from about 300 to about 350  
7 IU vitamin D; from about 13 to about 15 mg iron; from  
8 about 400 to about 420  $\mu$ g folic acid; from about 2 to  
9 about 6  $\mu$ g vitamin B<sub>12</sub>; from about 50 to about 65 mg  
10 vitamin B<sub>6</sub>; from about 75 to about 100  $\mu$ g chromium; from  
11 about 200 to about 300 IU vitamin E; from about 200 to  
12 about 300 mg vitamin C; and from about 12 to about 17 mg  
13 phytoestrogen in admixture with a biologically acceptable  
14 carrier.

1        Claim 10. The dietary supplement of claim 6 wherein  
2 said supplement comprises about 300 mg calcium, about 150  
3 mg magnesium, about 2 mg boron, about 2 mg copper, about  
4 3 mg manganese, about 12 mg zinc, about 300 IU vitamin D,  
5 about 15 mg iron, about 400  $\mu$ g folic acid, about 2  $\mu$ g  
6 vitamin B<sub>12</sub>, about 50 mg vitamin B<sub>6</sub>, about 75  $\mu$ g chromium,  
7 about 200 IU vitamin E, about 200 mg vitamin C, and about  
8 15 mg phytoestrogen.

1        Claim 11. A dietary supplement for supplementing  
2 the nutritional needs of post-menopausal women comprising  
3 about 200 to about 1500 mg calcium, about 150 to about  
4 250 mg magnesium, about 2.5 to about 3.5 mg boron, about  
5 2.5 to about 3.5 mg copper, about 4.4 to about 5.6 mg  
6 manganese, about 15 to about 18 mg zinc, about 300 to  
7 about 800 IU vitamin D, about 5 to about 10 mg iron,  
8 about 400 to about 440  $\mu$ g folic acid, about 2 to about 18  
9  $\mu$ g vitamin B<sub>12</sub>, about 1.6 to about 10 mg vitamin B<sub>6</sub>, about

10. 100 to about 200  $\mu$ g chromium, about 350 to about 800 IU  
11 vitamin E, about 300 to about 1000 mg vitamin C and about  
12 10 to less than 50 mg phytoestrogen in admixture with a  
13 biologically acceptable carrier.

1 Claim 12. The dietary supplement of claim 11 which  
2 further comprises from about 1200 to about 2000 RE  
3 preformed vitamin A and mixed carotenoids.

1 Claim 13. The dietary supplement of claim 11  
2 wherein said supplement is formulated in tablet, powder,  
3 liquid, capsule or gel form, or dietary bar.

1 Claim 14. The dietary supplement of claim 11  
2 wherein said supplement comprises about 300 to about 500  
3 mg calcium, about 150 to about 200 mg magnesium, about  
4 2.7 to about 3.3 mg boron, about 2.7 to about 3.3 mg  
5 copper, about 4.6 to about 5.4 mg manganese, about 15 to  
6 about 17 mg zinc, about 350 to about 400 IU vitamin D,  
7 about 8 to about 10 mg iron, about 400 to about  
8 420  $\mu$ g folic acid, about 2 to about 8  $\mu$ g vitamin B<sub>12</sub>,  
9 about 1.6 to about 3.2 mg vitamin B<sub>6</sub>, about 100 to about  
10 150  $\mu$ g chromium, about 350 to about 450 IU vitamin E,  
11 about 350 to about 450 mg vitamin C and about 12 to about  
12 17 mg phytoestrogen in admixture with a biologically  
13 acceptable carrier.

1 Claim 15. The dietary supplement of claim 11  
2 wherein said supplement comprises about 400 mg calcium,  
3 about 200 mg magnesium, about 3 mg boron, about 3 mg  
4 copper, about 5 mg manganese, about 15 mg zinc, about 400  
5 IU vitamin D, about 10 mg iron, about 400  $\mu$ g folic acid,  
6 about 2  $\mu$ g vitamin B<sub>12</sub>, about 1.6 mg vitamin B<sub>6</sub>, about 100  
7  $\mu$ g chromium, about 400 IU vitamin E, about 400 mg vitamin  
8 C, and about 15 mg phytoestrogen in admixture with a

9 biologically acceptable carrier.

1 Claim 16. A method for supplementing the dietary  
2 needs in an adult female comprising orally administering  
3 to a pre-perimenopausal, perimenopausal and menopausal or  
4 post-menopausal woman an effective amount of a life stage  
5 appropriate dietary supplement for each life stage  
6 throughout her life.

1 Claim 17. The method of claim 16 wherein the  
2 dietary supplement is selected from the group consisting  
3 of a Stage I dietary supplement for supplementing the  
4 dietary needs of pre-perimenopausal women and preventing  
5 or reducing risk of fetal neural tube defects, iron  
6 deficiency anemia, PMS, osteoporosis, at least one form  
7 of cancer, cervical dysplasia and coronary heart disease  
8 comprising effective amounts of calcium, magnesium,  
9 copper, boron, manganese, zinc, vitamin D, iron, folic  
10 acid, vitamin B<sub>12</sub>, vitamin B<sub>6</sub>, chromium, vitamin E,  
11 vitamin C and phytoestrogen in admixture with a  
12 biologically acceptable carrier; a Stage II dietary  
13 supplement for supplementing the dietary needs of  
14 perimenopausal and menopausal women and preventing or  
15 reducing the risk of PMS, symptoms of menopause, fetal  
16 neural tube defects, iron deficiency anemia,  
17 osteoporosis, at least one form of cancer, cervical  
18 dysplasia, and coronary heart disease comprising  
19 effective amounts of calcium, magnesium, copper, boron,  
20 manganese, zinc, vitamin D, iron, folic acid, vitamin B<sub>12</sub>,  
21 vitamin B<sub>6</sub>, chromium, vitamin E, vitamin C and  
22 phytoestrogen in admixture with a biologically acceptable  
23 carrier; and a Stage III dietary supplement for  
24 supplementing the dietary needs of post-menopausal women  
25 and preventing or reducing the risk of coronary heart  
26 disease, at least one form of cancer, cervical dysplasia

27 and osteoporosis comprising effective amounts of calcium,  
28 magnesium, copper, boron, manganese, zinc, vitamin D,  
29 iron, folic acid, vitamin B<sub>12</sub>, vitamin B<sub>6</sub>, chromium,  
30 vitamin E, vitamin C and phytoestrogen in admixture with  
31 a biologically acceptable carrier.

1 Claim 18. The method of claim 17 wherein

2 (A) the Stage I dietary supplement comprises about  
3 200 to about 500 mg calcium, about 100 to about 200 mg  
4 magnesium, about 0.5 to about 1.5 mg boron, about 0.5 to  
5 about 1.5 mg copper, about 2 to about 2.6 mg manganese,  
6 about 10 to about 13 mg zinc, about 200 to about 300 IU  
7 vitamin D, about 12 to about 18 mg iron, about 400 to  
8 about 440 µg folic acid, about 2 to about 10 µg vitamin  
9 B<sub>12</sub>, about 50 to about 100 mg vitamin B<sub>6</sub>, about 50 to  
10 about 100 µg chromium, about 100 to about 200 IU vitamin  
11 E, about 100 to about 1000 mg vitamin C and about 8 to  
12 less than 50 mg phytoestrogen;

13 (B) the Stage II dietary supplement comprises from  
14 about 200 to about 1000 mg calcium; from about 100 to  
15 about 200 mg magnesium; from about 1.5 to about 2.5 mg  
16 boron; from about 1.5 to about 2.5 mg copper; from about  
17 2.4 to about 3.6 mg manganese; from about 12 to about 15  
18 mg zinc; from about 300 to about 400 IU vitamin D; from  
19 about 10 to about 15 mg iron; from about 400 to about 440  
20 µg folic acid; from about 2 to about 15 µg vitamin B<sub>12</sub>;  
21 from about 50 to about 100 mg vitamin B<sub>6</sub>; from about 75 to  
22 about 200 µg chromium; from about 200 to about 400 IU  
23 vitamin E; from about 200 to about 1000 mg vitamin C; and  
24 from about 10 to less than 50 mg phytoestrogen; and

25 (C) the Stage III dietary supplement comprises  
26 about 200 to about 1500 mg calcium, about 150 to about  
27 250 mg magnesium, about 2.5 to about 3.5 mg boron, about  
28 2.5 to about 3.5 mg copper, about 4.4 to about 5.6 mg  
29 manganese, about 15 to about 18 mg zinc, about 300 to

30 about 800 IU vitamin D, about 5 to about 10 mg iron,  
31 about 400 to about 440  $\mu$ g folic acid, about 2 to about 18  
32  $\mu$ g vitamin B<sub>12</sub>, about 1.6 to about 10 mg vitamin B<sub>6</sub>, about  
33 100 to about 200  $\mu$ g chromium, about 350 to about 800 IU  
34 vitamin E, about 300 to about 1000 mg vitamin C and about  
35 10 to less than 50 mg phytoestrogen.

1 Claim 19. The method of claim 18 wherein an  
2 appropriate life stage dietary supplement is administered  
3 during at least two life stages of the woman.

1 Claim 20. The method of claim 18 wherein each of  
2 the life stage appropriate dietary supplements is  
3 administered throughout the appropriate life stage of the  
4 woman.

1 Claim 21. The method of claim 18 wherein the life  
2 stage appropriate dietary supplement is administered in  
3 the form of a tablet, powder, liquid, capsule or gel  
4 form, or dietary bar.

1 Claim 22. The method of claim 18 wherein the Stage  
2 I dietary supplement is administered to the woman  
3 throughout the pre-perimenopausal life stage of the  
4 woman.

1 Claim 23. The method of claim 18 wherein the Stage  
2 II dietary supplement is administered to the woman  
3 throughout the perimenopausal and menopausal life stage  
4 of the woman.

1 Claim 24. The method of claim 18 wherein the Stage  
2 III dietary supplement is administered to the woman  
3 throughout the post-menopausal life stage of the woman.

1           Claim 25. The method of claim 18 wherein

2           (A) the Stage 1 dietary supplement comprises about  
3 200 to about 300 mg calcium, about 100 to about 150 mg  
4 magnesium, about 0.7 to about 1.3 mg boron, about 0.7 to  
5 about 1.3 mg copper, about 2 to about 2.4 mg manganese,  
6 about 10 to about 12 mg zinc, about 200 to about 250 IU  
7 vitamin D, about 16 to about 18 mg iron, about 400 to  
8 about 420  $\mu$ g folic acid, about 2 to about 4  $\mu$ g vitamin  
9 B<sub>12</sub>, about 50 to about 65 mg vitamin B<sub>6</sub>, about 50 to about  
10 75  $\mu$ g chromium, about 100 to about 150 IU vitamin E,  
11 about 100 to about 150 mg vitamin C and about 8 to about  
12 12 mg phytoestrogen;

13           (B) the Stage II dietary supplement comprises from  
14 about 300 to about 400 mg calcium; from about 100 to  
15 about 150 mg magnesium; from about 1.7 to about 2.3 mg  
16 boron; from about 1.7 to about 2.3 mg copper; from about  
17 2.6 to about 3.4 mg manganese; from about 12 to about 14  
18 mg zinc; from about 300 to about 350 IU vitamin D; from  
19 about 13 to about 15 mg iron; from about 400 to about 420  
20  $\mu$ g folic acid; from about 2 to about 6  $\mu$ g vitamin B<sub>12</sub>;  
21 from about 50 to about 65 mg vitamin B<sub>6</sub>; from about 75 to  
22 about 100  $\mu$ g chromium; from about 200 to about 300 IU  
23 vitamin E; from about 200 to about 300 mg vitamin C; and  
24 from about 12 to about 17 mg phytoestrogen; and

25           (C) the Stage III dietary supplement comprises  
26 about 300 to about 500 mg calcium, about 150 to about 200  
27 mg magnesium, about 2.7 to about 3.3 mg boron, about 2.7  
28 to about 3.3 mg copper, about 4.6 to about 5.4 mg  
29 manganese, about 15 to about 17 mg zinc, about 350 to  
30 about 400 IU vitamin D, about 8 to about 10 mg iron,  
31 about 400 to about 420  $\mu$ g folic acid, about 2 to about 8  
32  $\mu$ g vitamin B<sub>12</sub>, about 1.6 to about 3.2 mg vitamin B<sub>6</sub>,  
33 about 100 to about 150  $\mu$ g chromium, about 350 to about  
34 450 IU vitamin E, about 350 to about 450 mg vitamin C and  
35 about 12 to about 17 mg phytoestrogen.



1           Claim 26. The method of claim 18 wherein

2           (1) the Stage I dietary supplement comprises about  
3   200 mg calcium, about 100 mg magnesium, about 1 mg boron,  
4   about 1 mg copper, about 2 mg manganese, about 10 mg  
5   zinc, about 200 IU vitamin D, about 18 mg iron, about 400  
6    $\mu$ g folic acid, about 2  $\mu$ g vitamin B<sub>12</sub>, about 50 mg vitamin  
7   B<sub>6</sub>, about 50  $\mu$ g chromium, about 100 IU vitamin E, about  
8   100 mg vitamin C and about 10 mg phytoestrogen;

9           (2) the Stage II dietary supplement comprises about  
10   300 mg calcium, about 150 mg magnesium, about 2 mg boron,  
11   about 2 mg copper, about 3 mg manganese, about 12 mg  
12   zinc, about 300 IU vitamin D, about 15 mg iron, about 400  
13    $\mu$ g folic acid, about 2  $\mu$ g vitamin B<sub>12</sub>, about 50 mg vitamin  
14   B<sub>6</sub>, about 75  $\mu$ g chromium, about 200 IU vitamin E, about  
15   200 mg vitamin C, and about 15 mg phytoestrogen; and

16          (3) the Stage III dietary supplement comprises  
17   about 400 mg calcium, about 200 mg magnesium, about 3 mg  
18   boron, about 3 mg copper, about 5 mg manganese, about 15  
19   mg zinc, about 400 IU vitamin D, about 10 mg iron, about  
20   400  $\mu$ g folic acid, about 2  $\mu$ g vitamin B<sub>12</sub>, about 1.6 mg  
21   vitamin B<sub>6</sub>, about 100  $\mu$ g chromium, about 400 IU vitamin E,  
22   about 400 mg vitamin C, and about 15 mg phytoestrogen.

1           Claim 27. A method for preventing or reducing risk  
2   of at least one form of cancer, cervical dysplasia,  
3   osteoporosis and coronary heart disease comprising orally  
4   administering to a pre-perimenopausal, perimenopausal and  
5   menopausal, and/or post-menopausal woman an effective  
6   amount of a life stage appropriate dietary supplement for  
7   each life stage throughout her life.

1           Claim 28. The method of claim 27 wherein  
2   administration of the life stage appropriate dietary  
3   supplement is continued throughout at least two life  
4   stages.

5           Claim 29. A method for preventing or reducing risk  
6 of iron deficiency anemia, PMS and fetal neural tube  
7 defects comprising administering to a pre-perimenopausal  
8 woman an effective amount of a life stage appropriate  
9 dietary supplement.

1           Claim 30. A method for preventing or reducing risk  
2 of PMS, symptoms of menopause, coronary heart disease,  
3 some cancers, cervical dysplasia and osteoporosis  
4 comprising administering to a perimenopausal or  
5 menopausal woman an effective amount of a life stage  
6 appropriate dietary supplement.

1           Claim 31. A method for preventing or reducing risk  
2 of coronary heart disease, at least one form of cancer  
3 and osteoporosis comprising administering to a post-  
4 menopausal woman an effective amount of a life stage  
5 appropriate dietary supplement.

1           Claim 32. A series of nutritional supplements  
2 formulated for the lifestage associated nutritional needs  
3 of a woman, comprising at least two of

4           (A) a nutritional supplement formulated for the  
5 preperimenopausal lifestage;

6           (B) a nutritional supplement formulated for the  
7 perimenopausal and menopausal lifestage; and

8           (C) a nutritional supplement formulated for the  
9 post-menopausal lifestage;

10           whereby the changing nutritional needs of a  
11 woman are supplemented.

1           Claim 33. A series of nutritional supplements  
2 according to claim 32 wherein

3           (A) the nutritional supplement for the  
4 preperimenopausal lifestage comprises a composition for

5 supplementing the dietary needs of preperimenopausal  
6 women and preventing or reducing risk of fetal neural  
7 tube defects, iron deficiency anemia, PMS, osteoporosis,  
8 at least one form of cancer, cervical dysplasia and  
9 coronary heart disease comprising effective amounts of  
10 calcium, magnesium, copper, boron, manganese, zinc,  
11 vitamin D, iron, folic acid, vitamin B<sub>12</sub>, vitamin B<sub>6</sub>,  
12 chromium, vitamin E, vitamin C and phytoestrogen in  
13 admixture with a biologically acceptable carrier;  
14 (B) the nutritional supplement for the  
15 perimenopausal and menopausal lifestage comprises a  
16 composition for supplementing the dietary needs of  
17 perimenopausal and menopausal women and preventing or  
18 reducing the risk of PMS, symptoms of menopause, fetal  
19 neural tube defects, iron deficiency anemia,  
20 osteoporosis, at least one form of cancer, cervical  
21 dysplasia, and coronary heart disease comprising  
22 effective amounts of calcium, magnesium, copper, boron,  
23 manganese, zinc, vitamin D, iron, folic acid, vitamin B<sub>12</sub>,  
24 vitamin B<sub>6</sub>, chromium, vitamin E, vitamin C and  
25 phytoestrogen in admixture with a biologically acceptable  
26 carrier; and  
27 (C) the nutritional supplement for the post-  
28 menopausal lifestage comprises a composition for  
29 supplementing the dietary needs of post-menopausal women  
30 and preventing or reducing the risk of coronary heart  
31 disease, at least one form of cancer, cervical dysplasia  
32 and osteoporosis comprising effective amounts of calcium,  
33 magnesium, copper, boron, manganese, zinc, vitamin D,  
34 iron, folic acid, vitamin B<sub>12</sub>, vitamin B<sub>6</sub>, chromium,  
35 vitamin E, vitamin C and phytoestrogen in admixture with  
36 a biologically acceptable carrier.

1 Claim 34. A series of nutritional supplements  
2 according to claim 33, wherein

3 (A) the composition for the preperimenopausal  
4 lifestage comprises about 200 to about 500 mg calcium,  
5 about 100 to about 200 mg magnesium, about 0.5 to about  
6 1.5 mg boron, about 0.5 to about 1.5 mg copper, about 2  
7 to about 2.6 mg manganese, about 10 to about 13 mg zinc,  
8 about 200 to about 300 IU vitamin D, about 12 to about 18  
9 mg iron, about 400 to about 440  $\mu$ g folic acid, about 2 to  
10 about 10  $\mu$ g vitamin B<sub>12</sub>, about 50 to about 100 mg vitamin  
11 B<sub>6</sub>, about 50 to about 100  $\mu$ g chromium, about 100 to about  
12 200 IU vitamin E, about 100 to about 1000 mg vitamin C  
13 and about 8 to less than 50 mg phytoestrogen in admixture  
14 with a biologically acceptable carrier;

15 (B) the composition for the perimenopausal and  
16 menopausal lifestage comprises from about 200 to about  
17 1000 mg calcium; from about 100 to about 200 mg  
18 magnesium; from about 1.5 to about 2.5 mg boron; from  
19 about 1.5 to about 2.5 mg copper; from about 2.4 to about  
20 3.6 mg manganese; from about 12 to about 15 mg zinc; from  
21 about 300 to about 400 IU vitamin D; from about 10 to  
22 about 15 mg iron; from about 400 to about 440  $\mu$ g folic  
23 acid; from about 2 to about 15  $\mu$ g vitamin B<sub>12</sub>; from about  
24 50 to about 100 mg vitamin B<sub>6</sub>; from about 75 to about 200  
25  $\mu$ g chromium; from about 200 to about 400 IU vitamin E;  
26 from about 200 to about 1000 mg vitamin C; and from about  
27 10 to less than 50 mg phytoestrogen in admixture with a  
28 biologically acceptable carrier; and

29 (C) the composition for the post-menopausal  
30 lifestage comprises about 200 to about 1500 mg calcium,  
31 about 150 to about 250 mg magnesium, about 2.5 to about  
32 3.5 mg boron, about 2.5 to about 3.5 mg copper, about 4.4  
33 to about 5.6 mg manganese, about 15 to about 18 mg zinc,  
34 about 300 to about 800 IU vitamin D, about 5 to about 10  
35 mg iron, about 400 to about 440  $\mu$ g folic acid, about 2 to  
36 about 18  $\mu$ g vitamin B<sub>12</sub>, about 1.6 to about 10 mg vitamin  
37 B<sub>6</sub>, about 100 to about 200  $\mu$ g chromium, about 350 to about

38 800 IU vitamin E, about 300 to about 1000 mg vitamin C  
39 and about 10 to less than 50 mg phytoestrogen in  
40 admixture with a biologically acceptable carrier.

1 Claim 35. A series of nutritional supplements  
2 according to claim 34 wherein

3 (A) the composition for the preperimenopausal  
4 lifestage comprises about 200 to about 300 mg calcium,  
5 about 100 to about 150 mg magnesium, about 0.7 to about  
6 1.3 mg boron, about 0.7 to about 1.3 mg copper, about 2  
7 to about 2.4 mg manganese, about 10 to about 12 mg zinc,  
8 about 200 to about 250 IU vitamin D, about 16 to about 18  
9 mg iron, about 400 to about 420  $\mu$ g folic acid, about 2 to  
10 about 4  $\mu$ g vitamin B<sub>12</sub>, about 50 to about 65 mg vitamin  
11 B<sub>6</sub>, about 50 to about 75  $\mu$ g chromium, about 100 to about  
12 150 IU vitamin E, about 100 to about 150 mg vitamin C and  
13 about 8 to about 12 mg phytoestrogen;

14 (B) the composition for the perimenopausal and  
15 menopausal lifestage comprises from about 300 to about  
16 400 mg calcium; from about 100 to about 150 mg magnesium;  
17 from about 1.7 to about 2.3 mg boron; from about 1.7 to  
18 about 2.3 mg copper; from about 2.6 to about 3.4 mg  
19 manganese; from about 12 to about 14 mg zinc; from about  
20 300 to about 350 IU vitamin D; from about 13 to about 15  
21 mg iron; from about 400 to about 420  $\mu$ g folic acid; from  
22 about 2 to about 6  $\mu$ g vitamin B<sub>12</sub>; from about 50 to about  
23 65 mg vitamin B<sub>6</sub>; from about 75 to about 100  $\mu$ g chromium;  
24 from about 200 to about 300 IU vitamin E; from about 200  
25 to about 300 mg vitamin C; and from about 12 to about 17  
26 mg phytoestrogen; and

27 (C) the composition for the post-menopausal  
28 lifestage comprises about 300 to about 500 mg calcium,  
29 about 150 to about 200 mg magnesium, about 2.7 to about  
30 3.3 mg boron, about 2.7 to about 3.3 mg copper, about 4.6  
31 to about 5.4 mg manganese, about 15 to about 17 mg zinc,

32 about 350 to about 400 IU vitamin D, about 8 to about 10  
33 mg iron, about 400 to about 420  $\mu$ g folic acid, about 2 to  
34 about 8  $\mu$ g vitamin B<sub>12</sub>, about 1.6 to about 3.2 mg vitamin  
35 B<sub>6</sub>, about 100 to about 150  $\mu$ g chromium, about 350 to about  
36 450 IU vitamin E, about 350 to about 450 mg vitamin C and  
37 about 12 to about 17 mg phytoestrogen.

1 Claim 36. A series of nutritional supplements  
2 according to claim 35 wherein

3 (A) the composition for the preperimenopausal  
4 lifestage comprises about 200 mg calcium, about 100 mg  
5 magnesium, about 1 mg boron, about 1 mg copper, about 2  
6 mg manganese, about 10 mg zinc, about 200 IU vitamin D,  
7 about 18 mg iron, about 400  $\mu$ g folic acid, about 2  $\mu$ g  
8 vitamin B<sub>12</sub>, about 50 mg vitamin B<sub>6</sub>, about 50  $\mu$ g chromium,  
9 about 100 IU vitamin E, about 100 mg vitamin C and about  
10 10 mg phytoestrogen;

11 (B) the composition for the perimenopausal and  
12 menopausal lifestage comprises about 300 mg calcium,  
13 about 150 mg magnesium, about 2 mg boron, about 2 mg  
14 copper, about 3 mg manganese, about 12 mg zinc, about 300  
15 IU vitamin D, about 15 mg iron, about 400  $\mu$ g folic acid,  
16 about 2  $\mu$ g vitamin B<sub>12</sub>, about 50 mg vitamin B<sub>6</sub>, about 75  
17  $\mu$ g chromium, about 200 IU vitamin E, about 200 mg vitamin  
18 C, and about 15 mg phytoestrogen; and

19 (C) the composition for the post-menopausal  
20 lifestage comprises about 400 mg calcium, about 200 mg  
21 magnesium, about 3 mg boron, about 3 mg copper, about 5  
22 mg manganese, about 15 mg zinc, about 400 IU vitamin D,  
23 about 10 mg iron, about 400  $\mu$ g folic acid, about 2  $\mu$ g  
24 vitamin B<sub>12</sub>, about 1.6 mg vitamin B<sub>6</sub>, about 100  $\mu$ g  
25 chromium, about 400 IU vitamin E, about 400 mg vitamin C,  
26 and about 15 mg phytoestrogen.

1           Claim 37. A series of nutritional supplements  
2 according to claim 34 wherein the compositions are in the  
3 form of a tablet, powder, liquid, capsule or gel form, or  
4 dietary bar.

1           Claim 38. A series of nutritional supplements  
2 according to claim 35 wherein the compositions are in the  
3 form of a tablet, powder, liquid, capsule or gel form, or  
4 dietary bar.

1           Claim 39. A series of nutritional supplements  
2 according to claim 36 wherein the compositions are in the  
3 form of a tablet, powder, liquid, capsule or gel form, or  
4 dietary bar.

1           Claim 40. A series of nutritional supplements  
2 according to claim 34 wherein the composition for the  
3 preperimenopausal lifestage further comprises from about  
4 400 to about 1200 RE preformed vitamin A and mixed  
5 carotenoids.

1           Claim 41. A series of nutritional supplements  
2 according to claim 34 wherein the composition for the  
3 perimenopausal and menopausal lifestage further comprises  
4 from about 800 to about 1600 RE preformed vitamin A and  
5 mixed carotenoids.

1           Claim 42. A series of nutritional supplements  
2 according to claim 34 wherein the composition for the  
3 postmenopausal lifestage further comprises from about  
4 1200 to about 2000 RE preformed vitamin A and mixed  
5 carotenoids.

1           Claim 43. A once daily dietary supplement for  
2 supplementing the nutritional needs of peri-menopausal

3 and/or menopausal women comprising less than about 20 mg  
4 phytoestrogen and a biologically acceptable carrier.

1 Claim 44. The dietary supplement of claim 43  
2 wherein the phytoestrogen is selected from the group  
3 consisting of genistin, glycitin, daidzin, malonyl  
4 daidzin, malonyl genistin, malonyl glycitin, acetyl  
5 glycitin, acetyl daidzin, acetyl genistin, genistein,  
6 glycitein, daidzein and mixtures thereof.

1 Claim 45. The dietary supplement of claim 43  
2 wherein the phytoestrogen comprises about 4.726 mg  
3 daidzin, about 1.257 mg glycitin, about 5.312 mg  
4 genistin, about 0.586 mg malonyl daidzin, about 0.217 mg  
5 malonyl glycitin, about 0.510 mg malonyl genistin, about  
6 0.670 mg acetyl daidzin, about 0.082 mg acetyl glycitin,  
7 about 0.595 mg acetyl genistin, about 0.0726 mg daidzein,  
8 about 0.062 mg glycitein, and about 0.060 mg genistein.

1 Claim 46. The dietary supplement of claim 43  
2 wherein the phytoestrogen comprises about 31 to 35 wt%  
3 daidzin, about 8 to 10 wt% glycitin, about 36 to 40 wt%  
4 genistin, about 3 to 5 wt% malonyl daidzin, about 0.5 to  
5 2.5 wt% malonyl glycitin, about 2.6 to 4.6 wt% malonyl  
6 genistin, about 3.7 to 5.7 wt% acetyl daidzin, about 0.1  
7 to 1.1 wt% acetyl glycitin, about 3.2 to 5.2 wt% acetyl  
8 genistin, about 0.1 to 1.0 wt% daidzein, about 0.1 to 1.0  
9 wt% glycitein, and about 0.1 to 0.9 wt% genistein.

1 Claim 47. The dietary supplement of claim 43  
2 wherein the phytoestrogen is obtained from whole soybean  
3 extract.

1 Claim 48. The dietary supplement of claim 43  
2 wherein the supplement comprises less than about 10 to



3 about 15 mg phytoestrogen.

1 Claim 49. The dietary supplement of claim 43  
2 wherein the supplement is formulated as a tablet,  
3 capsule, patch, gel, cream, chewing gum, powder,  
4 beverage, confectionary bar or cereal.

1 Claim 50. A method for supplementing the dietary  
2 needs of peri-menopausal and/or menopausal women said  
3 method comprising administering to the woman an amount of  
4 less than about 20 mg phytoestrogen per day.

1 Claim 51. The method of claim 50 wherein the amount  
2 of phytoestrogen administered is less than about 15 mg  
3 per day.

1 Claim 52. The method of claim 50 wherein the  
2 phytoestrogen is selected from the group consisting of  
3 genistin, glycitin, daidzin, malonyl daidzin, malonyl  
4 genistin, malonyl glycitin, acetyl glycitin, acetyl  
5 daidzin, acetyl genistin, genistein, glycitein, daidzein  
6 and mixtures thereof.

1 Claim 53. The method of claim 50 wherein the  
2 phytoestrogen is obtained from whole soybean extract.

1 Claim 54. The method of claim 50 wherein the  
2 phytoestrogen comprises about 4.726 mg daidzin, about  
3 1.257 mg glycitin, about 5.312 mg genistin, about 0.586  
4 mg malonyl daidzin, about 0.217 mg malonyl glycitin,  
5 about 0.510 mg malonyl genistin, about 0.670 mg acetyl  
6 daidzin, about 0.082 mg acetyl glycitin, about 0.595 mg  
7 acetyl genistin, about 0.0726 mg daidzein, about 0.062 mg  
8 glycitein, and about 0.060 mg genistein.

1           Claim 55. The method of claim 54 wherein the  
2 phytoestrogen comprises about about 31 to 35 wt% daidzin,  
3 about 8 to 10 wt% glycitin, about 36 to 40 wt% genistin,  
4 about 3 to 5 wt% malonyl daidzin, about .5 to 2.5 wt%  
5 malonyl glycitin, about 2.6 to 4.6 wt% malonyl genistin,  
6 about 3.7 to 5.7 wt% acetyl daidzin, about 0.1 to 1.1 wt%  
7 acetyl glycitin, about 3.2 to 5.2 wt% acetyl genistin,  
8 about 0.1 to 1.0 wt% daidzein, about 0.1 to 1.0 wt%  
9 glycitein, and about 0.1 to 0.9 wt% genistein.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/11932

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : Please See Extra Sheet.

US CL : Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC.

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Extra Sheet.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X - Y	MINDELL. "EARL MINDELL'S VITAMIN BIBLE". NEW YORK: WARNER BOOKS. 1991, PAGES 195-201, 216 AND 217.	50-53 _____ 16
X - Y	US 5,514,382 A (SULTENFUSS) 07 MAY 1996, SEE COLUMN 1, LINES 30-36, COLUMN 3, LINE 62 - COLUMN 4, LINE 2, COLUMN 4, LINE 9, COLUMN 5, LINES 60-62, COLUMN 6, LINES 20-21, 55 AND 56 AND COLUMN 7, LINES 6-8, 13, 14, 23 AND 24.	50-53 _____ 16 AND 27-31
Y	CZEIZEL ET AL. "PREVENTION OF THE FIRST OCCURENCE OF NEURAL-TUBE DEFECTS BY PERICONCEPTIONAL VITAMIN SUPPLEMENTATION" NEW ENGLAND JOURNAL OF MEDICINE. 24 DECEMBER 1992, VOL. 327, NO. 26, PAGES 1832-1835.	16 AND 27-31

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*B* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

26 SEPTEMBER 1997

Date of mailing of the international search report

16 OCT 1997

Name and mailing address of the ISA/US  
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**INTERNATIONAL SEARCH REPORT**International application No.  
PCT/US97/11932**C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GILMAN et al. "Goodman and Gilman's The Pharmacological Basis of Therapeutics". New York: Macmillan Publishing Co. 1980, 6th edition, pages 1249-1255.	27-31

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/11932

## A. CLASSIFICATION OF SUBJECT MATTER:

IPC (6):

A61K 31/07, 31/19, 31/28, 31/30, 31/34, 31/35, 31/44, 31/56, 31/59, 31/69, 31/295, 31/315, 31/435, 31/445, 31/495, 33/06, 33/08, 33/10, 33/22, 33/24, 33/26, 33/32 33/34, 35/78

## A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

424/630, 635, 639, 641, 643, 646, 647, 648, 655, 657, 660, 682, 687, 692, 697, 195.1; 514/ 64, 167, 168, 182, 249, 277, 290, 332, 334, 345, 456, 474, 492, 494, 499, 502, 557, 725

## B. FIELDS SEARCHED

Minimum documentation searched

Classification System: U.S.

424/630, 635, 639, 641, 643, 646, 647, 648, 655, 657, 660, 682, 687, 692, 697, 195.1; 514/ 64, 167, 168, 182, 249, 277, 290, 332, 334, 345, 456, 474, 492, 494, 499, 502, 557, 725